

Isocyanate Interim Guidance

References:

- (a) Air Force Letter of 1 Nov 94 - Armstrong Laboratory, Brooks Air Force Base, TX
- (b) Rudzinski, W.E., B. Dahlquist, S. Svejda, A. Richardson, T. Thomas, "Sampling and Analysis of Isocyanates in Spray Painting Operations," Am. Ind. Hyg. Assoc. J. 56:284-289 (1995)
- (c) "Toxicological Profile for Hexamethylene Diisocyanate," Agency for Toxic Substances and Disease Registry, August 1996 Draft.
- (d) Federal Register 2 Dec 96 pp 63726-63740
- (e) Silk, S.J., H. L. Hardy, "Control Limits for Isocyanates," Ann. Occup. Hyg., Vol. 27, No. 4, pp. 333-339, 1983.
- (f) NAVENVIRHLTHCEN ltr 5000 Ser 33B/5119 of 19 Nov 93
- (g) "1996 TLVs® and BEIs® Threshold Limit Values for Chemical Substances and Physical Agents," American Conference of Governmental Industrial Hygienists, 1996
- (h) Levine, S.P., K.J.D. Hillig, V. Dharmatajan, M.W. Spence, M.D. Baker, "Critical Review of Methods of Sampling, Analysis and Monitoring for TDI and MDI," Am. Ind. Hyg. Assoc. J. 56:581-589 (1995)
- (i) Miles Incorporated ltr of 29 Apr 94
- (j) PHONCON NAVENVIRHLTHCEN (Mr. Bishop)/Armstrong Laboratories (CAPT England) of 30 Jan 97
- (k) PHONCON NAVENVIRHLTHCEN (Mr. Bishop)/NIOSH (Dr. P. Schlecht) of 19 Feb 97
- (l) NEHC TM96-1 - "Industrial Hygiene Sampling Guide for Consolidated Industrial Hygiene Laboratories," Sep 96
- (m) Federal Register 19 Jan 89 pp 2332-2983

This document will present general issues regarding the workplace assessment for isocyanates with the current efforts in developing sampling/analytical methods and a recommended occupational exposure limit. Interim guidance for recommended personal protective equipment is also presented.

Brief Background

Isocyanates are chemicals that contain at least one isocyanate group in their structure. An isocyanate group contains one nitrogen, one carbon and one oxygen connected by double bonds. Chemicals containing two such groups are called diisocyanates. Common examples are,

toluene diisocyanate (TDI)
hexamethylene diisocyanate (HDI)

Enclosure (2)

These are called monomers since they can be made to react with one another and various other chemicals to form large chain-like compounds called polymers.

Polymeric isocyanates are used as precursors or intermediates in industrial applications. These are usually a mixture of monomers and polymerized isocyanates. For aromatic isocyanates, the functional group (NCO) in the polymers can be in the ortho-, meta- or para- positions. A prepolymer is synthesized by prereacting some or all of the NCO groups with polyols (molecules containing more than one OH group).

In polyurethanes, an activator is commonly used to form cross-linking. One common activator is 1,6-hexamethylene diisocyanate (HDI) and contains primarily the biuret or the isocyanurate of HDI and other higher weight oligomers. These products may contain only a small portion of free monomers of HDI. Most polyurethane paint systems will contain a prepolymer or polyisocyanate resin and is then mixed with a polyol when ready to apply.

HDI and TDI monomers evaporate relatively rapidly, resulting in potential vapor exposures in the work environment. Polymers or prepolymers of these monomers are formulated to reduce the evaporation rate and therefore reduce the inhalation potential. Various polymers and prepolymers are formulated based on other physical characteristics to ease the handling during use and the end characteristics of the cured product material.

Increasingly, polyurethane formulations contain only a small amount of unreacted monomers and a greater quantity of partially reacted polyisocyanates (note also that during use, the components have previously been mixed and are not fully reacted, i.e., they are uncured). From a workplace exposure standpoint, polymeric and prepolymer isocyanates will exist primarily as aerosols rather than vapors, especially when the product is sprayed, due to their high molecular weights. These aerosols may or may not be easy to sample (both from a sampling and lab analysis standpoint).

In the workplace, the atmosphere may contain some free monomer and mainly polymeric (or prepolymers) isocyanates. The isocyanates released in the air will depend on vapor pressures, composition of the polymer, particle size distribution and other dust generated (i.e., condensation nuclei and coating of small particles with unreacted material).

Health effects

Isocyanate exposure can cause skin, eye, nose, throat, and lung irritation. It can also lead to skin and lung sensitization. Some chronic decrement in lung function has been shown. Sensitization is a hyper-reactive (allergy-like) response to a substance, and may develop as a result of a large single exposure or from repeated exposures at lower levels.

The literature suggests that polyisocyanates can cause occupational asthma during spray painting (reference (a)). However, studies often do not differentiate between the adverse effects of exposure caused by the diisocyanate monomer and polyisocyanate because of the presence of both in the exposure (reference (b)) or the possibility of existing sensitization from previous exposures to monomers (reference (c)).

The Environmental Protection Agency (EPA) has published a significant new use final rule (reference (d)) for several chemical substances which were the subject of premanufacture notices in accordance with the Toxic Substances Control Act (TSCA). The final rule identified generic aliphatic polyisocyanates as materials which ***"cause skin sensitization and chronic lung toxicity in test animals."*** The rule also included generic polycyclic isocyanate and states ***"Similar chemicals have been shown to cause pulmonary sensitization and lung effects in test animals."***

Per reference (c), a susceptible population will exhibit a different or enhanced response to isocyanates than will most persons exposed to the same level in the environment. People may develop hypersensitization after only one exposure, either at a very low concentration for many hours or to a high concentration for just a few seconds.

Issues

1. What occupational exposure limit should be used?

Based on the significant exposure potential to polyisocyanate aerosols rather than individual monomers, workers may still be exposed to large amounts of potentially hazardous unreacted NCO groups. At this time, the Occupational Safety and Health Administration (OSHA) does not have permissible exposure limits (PELs) or short term exposure limits (STELs) for the polyisocyanates. The National Institute for Occupational Safety and Health (NIOSH) also has not established a recommended exposure limit (REL) for polyisocyanates (reference (a)). Also, the American Conference of Governmental Industrial Hygienists (ACGIH) do not have a Threshold Limit Value (TLV®) for polyisocyanates. The following sources provide occupational exposure standards for polyisocyanates:

Bayer (ex Miles, a manufacturer)	1 mg/m ³ STEL	0.5 mg/m ³ TWA
State of Oregon	1 mg/m ³ STEL	0.5 mg/m ³ TWA

The United Kingdom (reference (e)) bases limits in terms of unreacted NCO groups in the air (20 ug NCO/m³). This purports that unreacted NCO groups, regardless of the isocyanate compound, are the concern from a health perspective.

By reference (f), the Navy Environmental Health Center (NAVENVIRHLTHCEN) petitioned the Naval Medical Research Institute Detachment (Toxicology) to conduct research regarding the following:

1. Ascertain toxicity and relative risk of currently used isocyanates and their biuret, with particular attention to polyurethane paint systems.
2. Identify appropriate air sampling methods.
3. Propose appropriate exposure criteria for these isocyanate compounds and their biurets which do not currently have established exposure limits.

The response to the above request was a recommendation to use the TLVs® of reference (g) for the monomers and to calculate the polyisocyanate occupational exposure limits as outlined in reference (a). TLVs are presented for many isocyanate monomers. Knowing these compounds, their molecular weight, and the number of NCO groups present, a polyisocyanate exposure limit may be calculated per reference (a):

Example - The TLV for the MDI monomer is 0.051 mg/m³:

$$0.051 \text{ mg/m}^3 \times 84 \text{ g mw of NCO} / 250 \text{ g mw total MDI} = 0.017 \text{ mg NCO/m}^3 \text{ (17 ug NCO/m}^3\text{)}$$

Derived Limits Based on NCO Groups

Compound	Monomer TLV ug/m ³	Polyisocyanate Limit (Derived) ug NCO/m ³
HDI	34	17
Methyl Isocyanate	47	34.6
MDI	51	17.14
Methylene bis (4-cyclo-hexylisocyanate)	54	17.1
TDI	36	17.38
Isophorone diisocyanate	45	17.02

Overall Average 20.04 ug NCO/m³

Although the above polyisocyanate exposure limit calculation scheme establishes a good sound basis for assessing potential exposure risks using the established exposure limits for the monomers, NAVENVIRHLTHCEN do not recommend the adoption of the above based on:

- a. The problems in the airborne sampling (discussed in the next section), and,
- b. The lack of a risk/benefit evaluation using actual clinical outcomes from Navy workplaces.

2. What sampling technique and analysis method should be used to assess worker airborne exposures?

There are problems in measuring isocyanates in air from both chemical and physical perspectives. If we choose to measure the total reactive isocyanate groups in air, these groups will come from the monomers (if present) and the polymeric prepolymers or partially-reacted isocyanate materials. In non-spray operations, the main contribution of NCO groups will come from the monomers due to the higher vapor pressures and the higher "equivalent" NCO values (mass of NCO groups per molecular weight).

The amount of "free" isocyanates (or unreacted NCO groups) in air depend on the process emitting the aerosol. This includes the possible formation of combustion byproducts (stoichiometry of the polymer), particle size, and dust type (condensation nuclei for the vapor phases of monomers and prepolymers).

The analysis of prepolymers and partially reacted isocyanates pose problems using current methods. Also, pure standards have not been developed for all polymeric and partially reacted isocyanate products. There may also be problems or limitations using the chromatographic methods for the monomers (reference (h)). Methods for determining the free NCO groups have been based on forming derivatives with a reagent which should remain unchanged regardless of the compound and then detected using ultraviolet (UV) absorption or fluorescence of the reagent (reference (h)). Two reagents used have been methoxy-phenyl-piperazine and tryptamine.

For the assessment of aerosols with the ability to react with the derivitizing reagents, impingers are often used. Impinger efficiency for collection of isocyanates depends on flow rate, jet diameter and strike distance. At 1-2 liters per minute (lpm), the sampling efficiency for MDI aerosols falls off for aerosols having a mass median diameter of less than 1 μm . Thus, impinger sampling has been shown to underestimate methylene bisphenyl isocyanate (MDI) concentrations where the general aerosol sizes are in the range of 0.1 to 1 μm . Particle sizes of less than 0.05 μm behave like a vapor and the impinger becomes an efficient collector (reference (h)).

Workplace atmospheres may have heterogeneous aerosols containing two or more materials in a particle such as dust coated with prepolymer or isocyanate monomer or polymer. Impinger methods are useful reference methods when used in the laboratory. However, they are prone to spilling during and after sampling in the field, evaporation problems, contamination of glassware and spillage on the worker.

Analytical standards for the methods - Rather than preparing pure isocyanate derivatives, a known amount of isocyanate can be added to a known volume of derivatizing reagent in solution. It is then assumed that all of the isocyanate is derivatized. A problem can occur with the presence of moisture in the dimethyl sulfoxide (DMSO) solvent (if used in the procedure) and it can react with the isocyanate and bias the results. However, once the derivative is formed, moist DMSO will have no effect (reference (h)).

The following is a brief listing of current sampling methods with some identified problems:

NIOSH 2535 - uses p-nitrobenzyl-N-n-propylamine (nitro reagent) deposited on glass wool and packed in a sample tube. Not used.

NIOSH 5505 - uses 1 (2-methoxyphenyl)piperazine (MOPP) in an impinger - High pressure liquid chromatography (HPLC) analysis - Method retracted by NIOSH.

NIOSH 5521 - uses 1 (2-methoxyphenyl)piperazine (MOPP) in an impinger - HPLC analysis - analyzes for the derivative and is better than 5505. There are some problems with the UV absorption by the non-NCO parts of isocyanate molecule. Therefore, it is limited for total isocyanates but is quantitative for individual isocyanates. Note the particle/impinger problems discussed above.

NIOSH 5522 - uses tryptamine/DMSO in an impinger with HPLC analysis - This method determines the concentration of monomers and estimates air concentration of oligomers of specific diisocyanates - This method is not applicable to mixtures of different isocyanates and not recommended for personal breathing zone (PBZ) sampling due to the DMSO and potential spill/dermal exposure hazards.

OSHA 18 - Occupational Safety and Health Administration (OSHA) method - This method uses p-nitrobenzyl-N-n-propylamine (nitro reagent) in an impinger - HPLC analysis - Same problems as with 5521.

OSHA 42 and 47 - uses 1-(2-pyridyl)piperazine (PP) on a filter - solvent desorption and HPLC analysis - Filter must be stored in a refrigerator prior to use. OSHA 47 is basically identical to OSHA 42 with OSHA 42 for TDI, OSHA 47 for MDI. Some reports show that this method underestimates concentration depending on the aerosol size generated (reference (h)). Studies have shown that isocyanate aerosols losses can be reduced by

- 1) increasing the capture velocity (100-150 cm/sec),
- 2) adding diethyl phthalate and additional PP to the filter to provide a hydrophobic environment, and
- 3) desorb with PP reagent.

Loss on larger cassettes (25 or 35 mm filter) is significant compared to smaller cassettes (13 mm filter)(reference (h)). Studies on the 13 mm filters show no loss of the larger MDI particles demonstrated in the laboratory based tests of the 25-35 mm filters (reference (h)). Workplace moisture may react with the isocyanates and bias the results. Coating the filter with 2.0 mg of PP rather than 0.1 mg called for by the method, can provide accurate results on hot humid days when air volumes of up to 240 liters are taken. However, per reference (i), treated filters are not recommended for sampling airborne isocyanates during spray painting operations.

Iso-Check™ - Omega Specialty Instrument Co. - A dual filter for determining vapor and aerosols. A very involved analytical method with many reagents and glassware. Aerosol is

collected on a polytetrafluoroethylene filter (PTFE) and the vapor adsorbed on a second filter (glass fiber) impregnated with 9-(N-methylaminomethyl)anthracene (MAMA). The two analyses are performed separately. Prepolymers may react on first filter prior to the addition of the derivatizing reagent in long term sampling.

Per references (j) and (k), a joint study regarding side-by-side sampling of spray painting operations will be performed using various sampling methods. The study will evaluate the "field use" of OSHA Method 42, NIOSH Methods 5521 and 5522 and the Iso-Check™ Method. NIOSH shares NAVENVIRHLTHCEN concerns regarding assessment of the prepolymers and will remain in contact regarding the study. There is a strong desire to eliminate the need for impingers in field evaluations. NAVENVIRHLTHCEN will await for the results of this comparative study prior to a full recommendation of the optimum sampling and analytical method.

Interim Field Evaluation/Worker Protection Recommendations

The following recommendations for worksite assessment and worker protection are provided based on the above discussion and as interim guidance until further information is gathered to adequately determine an acceptable workplace exposure standard and a reliable validated and field acceptable air sampling analysis method. The recommendations are based on the referenced studies or documents and are intended to be prudent actions for inhalation and dermal exposure potentials considering the physical form of the exposure and the ability to quantitatively assess risk.

Mixing and brush applications - Includes worksite/equipment cleanup if not aerosolized:

Note: Each worksite should be evaluated to determine the actual or potential exposure to physical or chemical hazards based on the process being performed.

Airborne exposure assessment - Evaluate vapor exposures for the monomers or biuret that may be present in the paint (or isocyanate) system (for example, using OSHA 42/47 Method). Also evaluate organic vapors that may be present (consult reference (l)). Compare the results to the exposure limits of either reference (g) or (m).

Personal protective equipment - Evaluate the process for potential skin contact and/or splash hazards. An example of an ensemble for mixing and brush application:

- Full body disposable coveralls (Tyvek® or equivalent)
- Gloves (butyl rubber, nitrile or Viton®)
- Eye/face protection (chemical goggles/face shield if full face respirator is not required as based on air sampling assessments)
- Rubber shoes or shoe covers whenever there is a chance of footwear contamination from spillage or splashing
- Respirator - As determined by airborne exposure assessments of isocyanate and other organic vapor components of the paint system. Note that the minimum respirator for the protection against isocyanates is a supplied air respirator.

Spray Painting (including workers in the vicinity of spray painting operations): Includes the cleaning of the spray gun if aerosolized solvent is used.

Note: Each worksite should be evaluated to determine the actual or potential exposure to physical or chemical hazards based on the process being performed. Spray painting operations using dual component coatings shall only be conducted in areas designed for that purpose, such as a spray paint booth or spray room which ensures adequate ventilation and explosion protection (see OSHA 29 CFR 1910.94).

Airborne exposure assessment - Evaluate vapor exposures for the monomers or biuret that may be present in the paint (or isocyanate) system (for example, using OSHA 42/47 Method). Evaluate total airborne paint aerosol mass (gravimetric analysis). Also evaluate organic vapors that may be present (consult reference (1)). Compare the vapor results to the exposure limits of either reference (g) or (m). The total airborne aerosol results may be compared to the occupational exposure standard for polyisocyanates (interim guidance until the appropriate sampling method and airborne standard is determined): 1 mg/m³ STEL, 0.5 mg/m³ TWA. This is a conservative estimate of the mass of polyisocyanates assuming that all of the aerosol is the prepolymer.

Personal protective equipment - Evaluate the process for potential skin contact and/or splash hazards. An example of an ensemble for spray painting operations:

Full body disposable coveralls (Tyvek® or equivalent)

Gloves (butyl rubber, nitrile or Viton®)

Eye/face protection (chemical goggles/face shield if full face respirator is not required as based on air sampling assessments)

Rubber shoes or shoe covers whenever there is a chance of footwear contamination from spillage or splashing

Respirator - Full face air-supplied (Type C) respirator.